E UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:

Baker et al.

Docket No:

39780-2830P1C47

Serial No:

10/015,671

Group Art Unit:

1647

Filed:

December 11, 2001

Examiner:

Rachel B. Kapust

SECRETED AND TRANSMEMBRANE POLYPEPTIDES AND NUCLEIC For:

ACIDS ENCODING THE SAME

Commissioner for Patents Washington, D.C. 20231

DECLARATION OF WILLIAM WOOD, Ph.D. UNDER 37 CFR 1.131

I, William Wood, Ph.D. do hereby declare and say as follows:

- I am Director and Staff Scientist at the Department of Bioinformatics, of Genentech, 1. Inc., South San Francisco, CA 94080.
- 2. I am one of the inventors of the above-identified application.
- I have read and understood the claims pending in this application, and are aware that 3. the claims have been rejected as anticipated by U.S. Patent Publication No. 2003/0096951 (Jacobs et al., publication date May 22, 2003 and effective filing date August 14, 1998).
- I, along with other inventors of this application, conceived and reduced to practice the 4. polypeptide designated as PRO1244 (SEQ ID NO:130) claimed in the above-identified application in the United States prior to August 14, 1998.
- At the time the PRO1244 polypeptide was cloned and sequenced I was responsible for 5. overseeing the cloning of cDNAs which encoded novel polypeptides, including the cDNA that encoded PRO1244 polypeptide (SEQ ID NO:130) claimed in the aboveidentified application.
- A cDNA clone, referred to as DNA64883-1526 in the above-identified application, 6. was identified as encoding the PRO1244 polypeptide.
- 7. The full length of the cDNA clone is shown in Figure 73 of the above-identified application. The full-length cDNA sequence has 2213 nucleotide residues. The full

length of the PRO1244 peptide encoded by DNA64883-1526 is shown in Figure 74 of the above-identified application. The full-length PRO1244 polypeptide has 335 amino acid residues.

- 8. Copies of the pages from the GSeqEdit database which report the cloning and sequencing data for the PRO1244 polypeptide sequence and its encoding nucleic acid sequence are attached to this declaration (with the dates redacted) as Exhibit A.
- 9. The GSeqEdit report shows the full-length nucleic acid sequence for DNA-64883-1526 (identified as "DNA-64883") and the full-length PRO1244 polypeptide encoded by DNA 64883. Both the DNA-64883 and the PRO1244 polypeptide sequences were obtained prior to August 14, 1998.
- The DNA-64883 sequence shown in the GSeqEdit report is identical to that of SEQID NO: 129 disclosed in the above-identified application.
- 11. The beginning of the cDNA sequence corresponding to SEQ ID NO: 129 in the above-identified application is shown on page 1 of the GSeqEdit database report and the location of the first nucleotide is marked with "^insert starts here" and an arrow. The location of the last nucleotide corresponding to SEQ ID NO: 129 is shown on page 11 and is marked with an arrow.
- 12. The amino acid sequence shown in the GSeqEdit report is identical to that of SEQ ID NO: 130 disclosed in the above-identified application.
- 13. The first 26 amino acid residues of the PRO1244 polypeptide (SEQ ID NO:130) encoded by the cDNA (DNA-64883) are also shown on page 1 of the GSeqEdit report and the remaining 309 residues appear on pages 2-6 of the report.
- 14. Exhibit A clearly shows that both the full-length DNA-64883 sequence and the full-length PRO1244 polypeptide sequence disclosed in the above-identified application were obtained prior to August 14, 1998.
- 15. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information or belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and

the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful statements may jeopardize the validity of the application or any patent issued thereon.

William Wood

Date

SV 2037583 v1 6/9/04 1:21 PM (39780.2830) JUN 2 5 2004 6")

STATES PATENT AND TRADEMARK OFFICE

Applicants:

Baker et al.

Docket No:

39780-2830P1C47

Serial No:

10/015,671

Group Art Unit:

1647

Filed:

December 11, 2001

Examiner:

Rachel B. Kapust

For:

SECRETED AND TRANSMEMBRANE POLYPEPTIDES AND NUCLEIC ACIDS ENCODING THE SAME

Commissioner for Patents Washington, D.C. 20231

DECLARATION OF AUDREY GODDARD, Ph.D. UNDER 37 CFR 1.131

I, Audrey Goddard, Ph.D. do hereby declare and say as follows:

- 1. I am Senior Clinical Scientist at the Diagnostics, Development Sciences Department of Genentech, Inc., South San Francisco, CA 94080.
- 2. I am one of the inventors of the above-identified application.
- 3. I have read and understood the claims pending in this application, and are aware that the claims have been rejected as anticipated by U.S. Patent Publication No. 2003/0096951 (Jacobs *et al.*, publication date May 22, 2003 and effective filing date August 14, 1998).
- 4. I, along with other inventors of this application, conceived and reduced to practice the polypeptide designated as PRO1244 (SEQ ID NO:130) claimed in the above-identified application in the United States prior to August 14, 1998.
- 5. At the time the PRO1244 polypeptide was cloned and sequenced I was responsible for overseeing the sequencing of novel polypeptides, including the PRO1244 polypeptide (SEQ ID NO:130) claimed in the above-identified application.
- 6. A cDNA clone, referred to as DNA64883-1526 in the above-identified application, was identified as encoding the PRO1244 polypeptide.
- 7. The full length of the cDNA clone is shown in Figure 73 of the above-identified application. The full-length cDNA sequence has 2213 nucleotide residues. The full length of the PRO1244 peptide encoded by DNA64883-1526 is shown in Figure 74 of

- the above-identified application. The full-length PRO1244 polypeptide has 335 amino acid residues.
- 8. Copies of the pages from the GSeqEdit database which report the cloning and sequencing data for the PRO1244 polypeptide sequence and its encoding nucleic acid sequence are attached to this declaration (with the dates redacted) as Exhibit A.
- 9. The GSeqEdit report shows the full-length nucleic acid sequence for DNA-64883-1526 (identified as "DNA-64883") and the full-length PRO1244 polypeptide encoded by DNA 64883. Both the DNA-64883 and the PRO1244 polypeptide sequences were obtained prior to August 14, 1998.
- The DNA-64883 sequence shown in the GSeqEdit report is identical to that of SEQID NO: 129 disclosed in the above-identified application.
- 11. The beginning of the cDNA sequence corresponding to SEQ ID NO: 129 in the above-identified application is shown on page 1 of the GSeqEdit database report and the location of the first nucleotide is marked with "^insert starts here" and an arrow. The location of the last nucleotide corresponding to SEQ ID NO: 129 is shown on page 11 and is marked with an arrow.
- 12. The amino acid sequence shown in the GSeqEdit report is identical to that of SEQ ID NO: 130 disclosed in the above-identified application.
- 13. The first 26 amino acid residues of the PRO1244 polypeptide (SEQ ID NO:130) encoded by the cDNA (DNA-64883) are also shown on page 1 of the GSeqEdit report and the remaining 309 residues appear on pages 2-6 of the report.
- 14. Exhibit A clearly shows that both the full-length DNA-64883 sequence and the full-length PRO1244 polypeptide sequence disclosed in the above-identified application were obtained prior to August 14, 1998.
- 15. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information or belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001

of Title 18 of the United States Code and that such willful statements may jeopardize the validity of the application or any patent issued thereon.

Audrey Goddard

Date

SV 2037583 v1 6/15/04 3:03 PM (39780.2830)



Exhibit A to Declarations of Audrey Goddard and William Wood under 37 CFR 1.131

GSeqEdit Database Report



DNA64883 sheldens GSeqEdit DNA64883 goddarda GSeqEdit DNA64883 zemin GSeqEdit DNA64883 wiw GSegEdit >510 Sites [All Sites] >DNA64883 [Full]

>HBN64883.seq, sequenced at ABI/ACGT by Peter Ma and Ellson Chen >human ortholog of implantation-associated protein - Rattus

maeII/hpyC hpy991 mnll taiI fnu4HI/bsoFI hhal/cfol tseI bbvI hinPI haeII btgI/bstDSI nlaIII bstXI mslI bsaJI dsaI styl ncol tsp45I bsmAI maeIII tseI bstUI[M.hhaI-] fnuDII/mvnI hinPI acil nlaIII hhaI/cfoI bbvI bsh1236I fnu4HI/bsoFI thaI aval[M.taqI-] paeR7I mwoI tsp5091[M.ecoRI-] apol mwol bseRI mnlI taqI xhoI tliI smlI ecoRI

dde dsq

GCCTTAAGCC GAGCTCCTCG CTTGTACCGT CGCGCAACCG CCAAAACCAC ACAGAGACAC TGGTACCACC ACCGCGACGA GTAGCAAACG CTGCAAGGGA 1 CGGAATICGG CICGAGGAGC GAACAIGGCA GCGCGTIGGC GGTTITGGTG IGTCICIGIG ACCAIGGIGG IGGCGCIGCI CATCGTITGC GACGTICCCI **N** Q ပ ΛΙ A L L TWVV A S V MAARW

'Ainsert starts here

^MET

	E	mnli														aluI	=														
	alwN	alwNI[dcm-]	[-E													pvull	н														
	alw26I/bsmAI	61/b	smA]				bs	bsaXI			hp	hpy1881	H		_	msp.A	11/	mspAll/nspBII	II										bsmAI	AI	
101	101 CAGCCTCTGC CCAAAGAAAG AAGGAGATGG TGTTATCTGA AAAGGTTAGT CAGCTGATGG AATGGACTAA CAAAAGACCT GTAATAAGAA TGAATGGAGA	CTCI	ည	CAA	AGAA	AG A	AAGG	AGA.	IGG	TGTT	ATC	TGA	AAAG	GTT,	AGT	CAGO	TGA	IGG	AATG	GAC	L'AA	CAA	AGAC	E E	TAAT	'AAGA	IA T	BAATG	GAG	Æ	
	GTCG	GAGA	9	GTT	TCT	TC 1	TTCC	TCT	ACC	GTCGGAGACG GGTTTCTTTC TTCCTCTACC ACAATAGACT TTTCCAATCA GTCGACTACC TTACCTGATT GTTTTCTGGA CATTATTCTT ACTTACCTCT	TAG	ACT	TTT	CAA'	lCA	GTCG	ACT	ACC	TTAC	CTG	ATT	GTTI	TCTC	GA	ATTA	TTCI	T A(TTAC	CTC	£-i	
27	27 ASAQRKKEMV L	ഗ	Æ	O	×	, *	⋈	Σ	>	H	S	ഥ	×	>	S	a	Σ	M	3	H	z	×	M H	<i>></i>	H	œ	Σ	SEKVS QLME WTN KRP VIRM NGD	Ω		

	cac81	ij	hpyCH4V al	MANTIAC TCCGTTATCG TCATGTTCAC TGCTCTCCAA CTGCATAGAC AGTGTGTCGT TTGCAAGCAA	GTICAAGGCA GCGGAACACT TTCGGGGTGG CTCTTTAATG AGGCAATAGC AGTACAAGTG ACGAGAGGTT GACGTATCTG TCACACAGCA AACGTTCGTT	c
		cac8I	pyck	GCA	CGTI	N Y S V I V M F T A L.O LHRO C V V C K O
	bst4CI/hpyCH4III		٠.,	T II	A A	
	усн	ahdI/eam1105I		TCG	AGC	^
	I/hg	am11	н	TGT	ACAC	ر ن
	st4C	lI/e	SpR	. AG	, TC	_
	ă	ahc	hpyCH4V tspRI	AGA(TCT	2
٠			pyCH	SCAT	CGTA	H
			Ē	Ç	GA	,a
				CCAA	GGTT	0
٠.				CTCT	SAGA	1
	RI	Н		ŢĞ	ACC	Ø
	tspRI	btsI	H	TCAC	AGTG	H
			nlaIII	ATGT	raca	Ž.
			2	TC	AG	
				ATCG	IAGC	У
				GTT.	CAA	>
			H	TCC	AGG	S
	•		tsp5091	rTAC	AATG	>
			tsi	AAA.	TTT.	z
				GAG	CTC	×
				ACC	TGG	Д
				ည္သ	9999	Ωı
				AAG	TTC	¥
	•		•	TGA	ACT	×
)				TTG	BAAC	>
			16	ည္သ	9535	R I
			166Kdq	CGT	SCA	or.
			_	TIC	AAG	Fi I
				CAAG	STIC	×
				201 CAAGIICCGI CGCCIIGIGA AAGCCCCACC GAGA	_	60 KFR RLVK APP

```
btgI/bstDSI
                                                            nlaIII
                                                                                                                                        bsaJI
                                                                            styl
                                                                                                         dsaI
                                                                                           ncol
                                                                                                                        bssKI[dcm-] bsrI bsmI hphI
                                                                                                                                        apyI[dcm+] bpmI/gsuI[dcm-]
                                                                                                          tspRI
                                                                           ecoRII[dcm-]
                               scrFI[dcm-]
                                                                                                        bstNI bael
                                                                                         dsaV[dcm-]
                                               pspGI
                                                            mvaI
dpnII[dam-]
               dpn1[dam+]
                                             bstYI/xhoII
                                                                          alw261/bsmAI
                              alwI[dam-]
                                                                                         tsp5091[M.ecoRI-]
                                                            alwNI[dcm-]
                                                                                                        ecoRI pflMI[dcm-]
                                                                                                                        apol bsll[dcm-]
                                                                                                                                      mboli hpy188111
```

mbol/ndell[dam-]

sau3AI

ecoRII[dcm-]

dsaV[dcm-]

bstNI

bssKI[dcm-]
apyI[dcm+]

scrFI[dcm-]

pspGI

mvaI

301 GCTGATGAAG AATTCCAGAT CCTGGCAAAC TCCTGGCGAT ACTCCAGTGC ATTCACCAAC AGGATATTT TTGCCATGGT GGATTTTGAT GAAGGCTCTG CGACTACTIC TTAAGGICTA GGACCGITIG AGGACCGCIA TGAGGICACG TAAGTGGITG ICCTATAAAA AACGGIACCA CCTAAAACTA CITCCGAGAC

S

Œ

93 A D

(L)

Ω

tsp5091[M.ecoRI-]

ecoRI

hpyCH4V

apol

ecoNI

aluI nlaIII

bslI

aciI

ndeI

hphI

pslI

ტ 2

401 ATGTATITCA GATGCTAAAC ATGAAITCAG CTCCAACTIT CATCAACTIT CCTGCAAAAG GGAAACCCAA ACGGGGTGAT ACATATGAGI TACAGGTGCG TACATAAAGT CTACGATTTG TACTTAAGTC GAGGTTGAAA GTAGTTGAAA GGACGTTTTC CCTTTGGGTT TGCCCCACTA TGTATACTCA ATGTCCACGC maeIII II E 127

z

ഗ

Z

z

ddeI[M.aluI-]

sau3AI bspCNI

hpall mbol/ndell[dam-] cellI/espI

blpI/bpull02I scrFI[M.hpaII-]

dpnII[dam-] dpnI[dam+] nciI dsaV IInad aluI

sau96I bsmFI

nlaIV

bssKI alwI[dam-]

501 GGGTTTTTCA GCTGAGCAGA TTGCCCGGTG GATCGCCGAC AGAACTGATG TCAATATTAG AGTGATTAGA CCCCCAAATT ATGCTGGTCC CCTTATGTTG avall bsli tsp509I sspI mspAll/nspBII

CCCAAAAAGT CGACTCGTCT AACGGGCCAC CTAGCGGCTG TCTTGACTAC AGTTATAATC TCACTAATCT GGGGGTTTAA TACGACCAGG GGAATACAAC Σ H > œ G 160

fnu4HI/bsoFI aluI Inqq tseI bstF5I fokI tru9I tsp509I bsici bstBI taqI sful

CCTAACGAAA ACCGACAATA ACCACCTGAA CACATAGAAG CTTCTTCATT ATACCTTAAA GAGAAATTAT TTTGACCTAC CCGAAAACGT CGAAACAAA 601 GGATTGCTTT TGGCTGTTAT TGGTGGACTT GTGTATCTTC GAAGAAGTAA TATGGAATTT CTCTTTAATA AAACTGGATG GGCTTTTGCA GCTTTGTGT mwol hpyCH4V bsrI mseI apoI Ilodm Ilodm baeI

ပ ပ G 193

nlaIII	styI	ncol	dsaI	btgI/bs	saJI	CATGG	STACC	9	
_	st	č	ö	Ā	tsp5091 bsaJI	ratco	ATAG(H T G H V N Y I H G	
					509	II A	A T	×	
H					tsi	GAAT	CTTZ	z	
nlaIII	ы	H	ы	III		ATGI	TACA	>	
ci.	pcil	nspHI	Idsu	aflili	FI	S. C.	T.	Ħ	
					DSmFI	9990	ညည	Ŋ	
						ACA	TGI	H	
			bslI			ၓ	ဗ	,Li	
			Д	tfi	hinfI	MIC	TAG	PI PI	
				Ħ	2	AAG?	TTC	N P	
						C AT	T. TA	int.	
						ညည	9903	~ «	
					ndeI	ATAI	TAL	×	
			L		=	S	99	щ	
			sau96I	avaII		ACC	TGG	R G P P Y A H	
			Sa	ā	mnll	GAGG	CTCC	ტ	
					_	AA.	TI	α;	
						ATAI	TAT	H	
					nlaIV	AACC	rtgg	N	
					nla	25	S	_	
						ATGT	raca	35. 35.	
					121	CAA	GTT	a	
					m110	GGJ	\mathcal{C}	ڻ .	
					ahdI/eam1105I	ATCT	IAGA	ß	
					ahd	GAC	CTG	H	•
						TAT	ATA	Σ	
					38I	TGC	ACG	æ	
					cac8I	701 TTGTGCTTGC TATGACATCT GGTCAAATGT GGAACCATAT AAGAGGACCA CCATATGCCC ATAAGAATCC CCACACGGGA CATGTGAATT ATATCCATGG	AACACGAACG ATACIGTAGA CCAGITTACA CCTIGGIATA TICICCIGGI GGIATACGGG TATICITAGG GGIGIGCCCI GIACACITAA TATAGGIACC	227 VIAMTS GOMW	
						701	~	227	

	fnu4HI/bsoFI	hpy1	mnlI	801 AAGCAGTCAA GCCCAGTTTG TAGCTGAAAC ACACATTGTT CTTCTGTTTA ATGGTGGAGT TACCTTAGGA ATGGTGCTTT TATGTGAAGC TGCTACCTCT	TICGICAGIT CGGGICAAAC AICGACITIG IGIGIAACAA GAAGACAAAI IACCACCICA AIGGAAICCI IACCACGAAA AIACACIICG ACGAIGGAGA	V L L F N G G V T L G M V L L C E A A T S
tseI	u4HI	bbvI	н	JGC	ACG	Ø
ts	fn	qq	aluI	AAGC	ITCG	A
				GTG	CAC	<u> </u>
				TAT	ATA	C
		H		TTT	AAA	Η.
		/sac		GTGC	CACG	N N
		tII		ATG	TAC	Σ
	н	bsu36I/mstII/sauI		GGA	CCT	G
ddeI	eco811	3n36		TTA	SAAT	H
0	a	ğ	maeIII	TACC	ATG	€→
			mae	AGT	ĘŽ.	>
				TGG	ACC	Ŋ
		н		ATGG	TACC	G
		tru9I	mseI	TA	'AT	Z
		-	=	TGT	ACA	Ţ
			mboli	CTTC	SAAG	
			ď	TT.	AA (_
				ATTC	TAAC	⊢
				ACAC	TGTG	æ
				NAC.	rrg	E
			H	TGA	ACT	Œ
			aluI	TAGC	ATCG	4
				TG	AC.	>
			bsrI	AGTI	TCA	ह्म
٠			ps	ည္တင္တ	9990	O1
				AA C	TT	260 S. S. Q. A. Q. F. V. A. E. T. H.
				AGTC	rcag	0 5
				AGC	TCG	S.
)1 A	E	20
				9		5(

		IJ	()	(O
dpnI[dam+]	bstYI/xhoII	*	TCTAAATAT	AGATTTATA
dp	bst	bqlii	TATTTTAGA	ATAAAAATCT
sfani	fokI	bstF5I	GGATGCTCTC	CCTACGAGAG
	eco571	Ilodm	TICTICAGIL	AAGAAGTCAA
			TGTTGTATTA	ACAACATAAT
			GTATTGGACT	CATAACCTGA
			TGTGTGGCTG	ACACACCGAC
			AAAGATAATG	TTTCTATTAC
			TTGGAAAGCG	AACCTTTCGC
		nlaiii	901 GACATGGATA TTGGAAAGCG AAAGATAATG TGTGTGGCTG GTATTGGACT TGTTGTATTA TTCTTCAGTT GGATGCTCTC TATTTTTAGA TCTAAATATC	CTGTACCTAT AACCTTTCGC TTTCTATTAC ACACACCGAC CATAACCTGA ACAACATAAT AAGAAGTCAA CCTACGAGAG ATAAAAATCT AGATTTATAG
			901	ć

S

υ Σ

Œ

A V L

1 9

C V A

293 D M D I

mboI/ndeII[dam

sau3AI

dpnII[dam-]

bsmFI

bsrI sau96I

rsal nlaIV bpmI/gsuI[dcm-]

avaII

1001 ATGGCTACCC ATACAGCTTT CTGATGAGTT AAAAAGGTCC CAGAGATATA TAGACACTGG AGTACTGGAA ATTGAAAAAC GAAAATCGTG TGTGTTTGAA tsp5091 csp61 scal bsrI tspRI eco01091/draII **DPuMI** tru9I mseI aluI hpy188I

TACCGATGGG TATGTCGAAA GACTACTCAA ITTTTCCAGG GTCTCTATAT ATCTGTGACC TCATGACCTT TAACTTTTTG CTTTTAGCAC ACACAACTT

0 လ Σ н တ G

tru9I

tru9I mseI

tru9I tru9I ahaIII/draI

mbolI

1101 AAGAAGAATG CAACTTGTAT ATTTTGTATT ACCTCTTTTT TTCAAGTGAT TTAAATAGTT AATCATTTAA CCAAAGAAGA TGTGTAGTGC CTTAACAAGC ITCTICTIAC GITGAACAIA TAAAACAIAA TGGAGAAAAA AAGIICACIA AAITTAICAA ITAGIAAAII GGITICIICI ACACAICACG GAAITGIICG mseI mseI mseI

Swal

mnlI

mboll hpyCH4V

mnll

tru9I rsal tsp5091 tsp509I tru9I mbolI tspRI mnll tru91 bspCNI ddeI

mseI csp6I mseI earI/ksp632I mseI tsp5091 hpy1881 mnlI

1201 AATCCTCTGT CAAAATCTGA GGTATTTGAA AATAATTATC CTCTTAACCT TCTCTCCCA GTGAACTTTA TGGAACATTT AATTTAGTAC AATTAAGTAT TTAGGAGACA GTTTTAGACT CCATAAACTT TTATTAATAG GAGAATTGGA AGAGAGGGT CACTTGAAAT ACCTTGTAAA TTAAATCATG TTAATTCATA

tru9I

mseI

hpaI

1301 ATTATAAAAA TIGTAAAACT ACTACTITGT TITAGTTAGA ACAAAGCTCA AAACTACTTT AGTTAACTIG GTCATCTGAT TITATATIGC CTTATCCAAA taatatttit aacatittga tgatgaaaca aaatcaatct tgtttcgagt tttgatgaaa tcaattgaac cagtagacta aaatataacg gaataggttt bslI hincII/hindII hpy188I aluI tsp509I psil

					tsp5091[M.ecoRI-]	xmnI	ecoRI	asp700 aluI
scrFI[dcm-]	Igdsd	mvaI	ecoRII[dcm-]	dsaV[dcm-]	bstNI	bssKI[dcm-]	apyI[dcm+]	sexAI

bstF5I 1401 GAIGGGGAAA GIAAGICCIG ACCAGGIGII CCCACAIAIG CCIGIIACAG AIAACIACAI IAGGAAITCA IICTIAGCII CIICAICIII GIGIGGAIGI CTACCCCTIT CATICAGGAC IGGICCACAA GGGIGIAIAC GGACAAIGIC TAITGAIGIA AICCTIAAGI AAGAAICGAA GAAGIAGAAA CACACCIACA ddeI[M.aluI-] apoI maeIII ndeI hpy188III

fokI

mslI

Ilodm

						•
	rmal ddel	H4IV	pspc	mnlI	CCTC	SGGAG
	rmäI	maeII/hpyCH4IV	aflii maei bspC	bfaI	TCTAGG	AGATCO
bsp1286	bsiHKAI	I mae	aflii	mboli bmyl btri bfal mnli	GCACACG	cererec
[sq	ps	hpy1881	eco57I	ind II	IC AGA	AG TCT
			ecc	[oqu	ACCATTCT	TGGTAAGA
	81	•			AAAATGGAAC	TTTACCTIG
	hpy188I	Ilodm	bpuAI	nlaIII bbsI	regretrere	ACCAGAAGAC
					STGTGTCATG '	CACACAGTAC
				tsp5091	SAGAAATTAT (CTCTTTAATA (
					CTTTTGAGTA (SAAAACTCAT (
				sfaNI	CGCATCTTTC (CATATGAAAT GCGTAGAAAG GAAAACTCAT CTCTTTAATA CACACAGTAC ACCAGAAGAC TTTTACCTTG TGGTAAGAAG TCTCGTGTGC AGATCGGGAG
		bst217I	bst1107I	accI	1501 GTATACTITA CGCATCTITC CITITGAGIA GAGAAATIAI GIGIGICAIG IGGICITCIG AAAAIGGAAC ACCATICIIC AGAGCACACG ICIAGCCCIC	CATATGAAAT
					1501	

hgiAI/aspHI

taiI

tth11111/aspI

pleI

pflFI

mlyI

bpmI/gsuI[dcm-]

hinPI

hinfI

bsmAI bsmAI 1601 AGCAAGACAG TIGITICICC ICCICCITGC ATAITICCIA CIGCGCICCA GCCIGAGIGA TAGAGIGAGA CICIGICICA AAAAAAAGIA ICICIAAAIA TCGTTCTGTC AACAAAGAGG AGGAGGAACG TATAAAGGAT GACGCGAGGT CGGACTCACT ATCTCACTCT GAGACAGAGT TTTTTTCAT AGAGATTTAT

hhal/cfol bspCNI

bst4CI/hpyCH4III mnll hpyCH4V

bseRI mnlI bseRI

tsp45I

hphI

msel

tru9I

tfil

hinfi

xmnI

hincII/hindII

hpaI

tsp5091

asp700 hpy1881

msel bstEII

tru91 maeIII

STCCTAATAT TAAAGACGAA CTCATACCAC AATTGATGGA ACATAAATCT TTCTAAAGTC TAAGTAAGGT AGAGGAATCA AAAGAAAATT CCACTGGGTA 1701 CAGGATTATA ATTICTGCTT GAGTATGGTG TTAACTACCT TGTATTTAGA AAGATTTCAG ATTCATTCCA TCTCCTTAGT TTTCTTTAA GGTGACCCAT

maeIII ddeI[M.aluI-]

tspRI

haeIII/palI

nlaIII

tsp5091

maeIII

tsp45I

csp6I rsal

dde

GACACTATIT TTATATCGAA TCACGATITT AGTCACATIG AATATGIACC GGATTITACA AAGATGTTTA ATCTCAAACA GTGAATAAGG TAAACATGGA 1801 CIGIGATAAA AATATAGCTT AGTGCTAAAA TCAGTGTAAC TTATACATGG CCTAAAATGT TTCTACAAAT TAGAGTTTGT CACTTATTCC ATTTGTACCT

```
styl cac81
                                                                                                                                                                                                                                            haeIII/palI
                                                                                                                                                                                                                                            ddeI
                                                                                                                                                                       tsp45I
                                                                                                                                                                                     maeIII
                                                                                                                                                                                                                              pleI bslI[dcm-] hhaI/cfoI
                                                                                                                                                                                                                bssKI[dcm-] tspRI
                                                                                  mscI/ball[dcm-]
                             ecoRII[dcm-]
                                                                                                                                                                                                   hinPI
                                                                                                                                                         mval bssKI[dcm-]
                                                                                                                                                                                                                                           mlyI bsaJI apyI[dcm+]
                                          dsaV[dcm-]
                                                                     haeIII/palI
                                                                                                eaeI[dcm-]
                                                                                                                                                                       ecoRII[dcm-]
                                                                                                                            scrFI[dcm-]
pspGI
                                                        bstNI
                                                                                                                                                                                    dsaV[dcm-]
               mvaI
                                                                                                              cfrI
                                                                                                                                                                                                  bstni
                                                                                                                                           pspGI
                                                                                                                                                                                                                                           ddeI
```

scrFI[dcm-]

bssS hpy18

dpnII[d dpnI[da

mnll bsaJI

bspCNI

1901 AAGAGAAAAA TAGGCTCAGT TAGAAAAGGA CICCCTGGCC AGGCGCAGTG ACTTACGCCT GTAATCTCAG CACTTTGGGA GGCCAAGGCA GGCAGATCAC

hinfI apyI[dcm+] btsI

bspCNI

TICICITITI ATCCGAGICA ATCITITCCI GAGGGACCGG TCCGCGICAC IGAATGCGGA CATTAGAGIC GIGAAACCCI CCGGITCCGI CCGICIAGIG

mboI/nd sau3AI

2001 GAGGTCAGGA GTTCGAGACC ATCCTGGCCA ACATGGTGAA ACCCCGTCTC TACTAAAAT ATAAAATTA GCTGGGTGTG GTGGCAGGAG CCTGTAATCC aluI tsp509I bsmAI esp3I bsmBI hpy188III apy1[dcm+] hphI mscI/ball[dcm-] nlaIII hpy188III bsaI bstF5I haeIII/palI eaeI[dcm-] ecoRII[dcm-] bssKI[dcm-] scrFI[dcm-] dsaV[dcm-] taqI fokI cfrI bstNI pspGI mvaI bsmAI

ecoRII[dcm-] scrFI[dcm-] bssKI[dcm-] apyI[dcm+] dsaV[dcm-] pspGI bstNI mval dpnII[dam-] hpyCH4V mboI/ndeII[dam-] tspRI btsI sau3AI hpy188III ddeI hinfI tfiI **DSPCNI** ddeI

CICCAGICCI CAAGCICIGG IAGGACCGGI IGIACCACIT IGGGGCAGAG AIGAITITIA TAITITAAI CGACCCACAC CACCGICCIC GGACATIAGG

nlaIV

2101 CAGCTACACA GGAGGCTGAG GCACGAGAAT CACTTGAACT CAGGAGATGG AGGTTCAGT GAGCCGAGAT CACGCCACTG CACTCCAGCC TGGCAACAGA GTCGATGIGT CCTCCGACTC CGTGCTCTTA GTGAACTTGA GTCCTCTACC TCCAAAGTCA CTCGGCTCTA GTGCGGTGAC GTGAGGTCGG ACCGTTGTCT dpnI(dam+) bsgI bpmI/gsuI[dcm-]

tspRI

mnlI

bspCNI

mnli mnli bssSI

aluI

fnu4HI/bsoFI

haeIII/palI

mcrI

eagI/xmaIII/eclXI

eaeI

cfrI

rmaI

bsiEI

mael notI

hinfi mlyI

bsmAI

pleI

fnu4HI/bsoFI bfaI

acil acil

2201 GCGAGACTCC ATCTCAAAAA AAAAAAAAA AAAAAAAA AAAAAAGGG CGGCCGCCGA CTAGTGAGC

> length: 2269

accI (GTMKAC):

acil (CCGC):

aflii (ACRYGT):

ahalii (TTTAAA):

ahdi (GACNNNNGTC):

aluI (AGCT):

alw261 (CAGNNNCTG):

alwI (GGATCNNNN):

alwni (CAGNNNCTG):

apol (RAATTY):

apyI (CCWGG):

asp700 (GAANNNTTC):

aspHI (GWGCWC):

1150

278 714

101 316

318 530

101 316

1464 1749